

MAR 1 9 2001

K010052

TAB 9**SUMMARY OF SAFETY AND EFFECTIVENESS**

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Classification Name Bilirubin (total and unbound) in the neonate test system

Regulation Number 862.1113

Product Code MQM

Common/Usual Name Bilirubin Analyzer

Proprietary Name Bilichek Noninvasive Bilirubin Analyzer

Predicate Device Bilichek Noninvasive Bilirubin Analyzer (K983071)

Reason for submission Expanded claims

Substantial Equivalence

The Bilichek device has the following key similarities to the predicate devices:

- ☐ Intended use.
- ☐ Environment of use.
- ☐ Operating principle.
- ☐ Technology.

Respironics has determined that the differences from the predicate devices have no impact on the safety and effectiveness of the device. Design verification tests were performed on the Bilichek Bilirubin Analyzer as a result of the risk analysis and product requirements. All tests were verified to

meet the required acceptance criteria. In summary, the device described in this submission is substantially equivalent to the predicate devices.

The device complies with the applicable standards referenced in the Guidance for FDA Reviewers and Industry "Guidance for the Content of premarket Submissions for Software Contained in Medical Devices," May 1998.

Intended Use

The Bilichek Non-Invasive Bilirubin Analyzer is a computer assisted non-invasive transcutaneous bili-rubinometer, which is intended as an index to predict serum bilirubin levels prior to phototherapy (pre-phototherapy), during and post phototherapy in neonates, without regard to gender, gestational age, or bodyweight.

Device Description

The Bilichek provides a numerical measurement of predicted bilirubin count in mg/dL within a clinically beneficial range that has been correlated with total serum bilirubin concentration measured by High Performance Liquid Chromatography (HPLC). The device is intended for use in the hospital or institutional environment to assist clinicians in monitoring the status of neonates for the development of hyperbilirubinemia. Neonates whose Bilirubin test results are indicative of hyperbilirubinemia are evaluated by their physician(s) for appropriate patient management.

Accessories

The Bilichek includes the following accessories:

- ☐ Rechargeable Battery Packs
- ☐ Charger Base
- ☐ Power Supply w/ Power Cord
- ☐ BiliCal Calibration Tips

-- Continued on the next page. --

Operating Principle

The operating principle for the Bilichok non-Invasive Analyzer remains unchanged from the original Bilichok device, which was cleared under K983071. The reason for this submission is to expand the intended use to include use during phototherapy. The device works by directing white light into the skin of the newborn and measuring the intensity of the specific wavelengths that are returned. By understanding the spectral properties of the components within the skin, the device has been designed to eliminate the interfering components and measure the concentration of bilirubin.

Each photon has a characteristic wavelength. As light enters the skin tissue, it can collide with the structural components, such as collagen fibers. When a collision occurs, the photon loses energy and the direction of the travel is changed. This is called a scattering event. If enough of these events occur, the photon completely loses its energy and is absorbed. If a photon is scattered such that it is re-emitted from the skin it is reflected.

Photons with longer wavelengths (in the red region of the spectrum) are scattered less than photons with shorter wavelengths (in the blue region of the spectrum). This phenomena is called wavelength-dependent scattering and explain why the skin appears red when a bright light is shined through it. It is also one of the newborn's skin changes with advancing gestational and postnatal age. As the skin matures, it becomes thicker and there is keratinization of the cell membranes which increases the scattering of incident light.

Photons of specific wavelengths are also preferentially absorbed by certain molecules. By plotting the absorption against the wavelength, one can visualize characteristic absorption spectra of the particular molecules. The light reflected from the skin of neonates and collected by the Bilichok device is analyzed to generate a serum bilirubin measurement. The device takes an analysis of the following optical components:

1. The dermis provides a baseline optical density (OD) from the collected fraction of delivered light.
2. The melanin exerts an OD, which behaves as if it has zero contribution at 837 nanometers (nm) and increases linearly with shorter wavelengths.
3. The blood adds additional OD below 600 nm.
4. The bilirubin adds additional OD in the 460 (+/- 20 nm) range.

By utilizing the known spectral characteristics of each component, the contribution to the total OD can be sequentially subtracted until bilirubin is all that is remaining.

Functional Description

Bilichék Hand-Held Unit

The BiliCheck Hand-Held Unit consists of the following functional components:

1. **TRIGGER** button – The single button on the bottom of the unit is called **TRIGGER**. It is used to initiate calibration and patient measurement.
2. **FUNCTION** buttons – The two buttons on the top side are **FUNCTION** buttons. The blue button on the left is referred to as **F1**, and the green button on the right as **F2**. These are used to initiate non-routine functions such as set-up, changing time and date, etc.
3. BiliCal™ Individual Calibration Tip – This tip serves five purposes:
 - a) device calibration before each patient measurement,
 - b) protection of the fiber-optic probe,
 - c) protection of the surface of the calibration material,
 - d) positioning aid to ensure proper placement of the probe,
 - e) a clean surface for each patient measurement.
4. Display window – The display window shows the bilirubin measurement, time and date, audio and battery icons, Measurement Status Indicator (MSI) as well as other system and error messages.
5. Battery Pack – Located in the bottom portion of the handle, it provides the electrical energy to operate the various components.

Charger Base

The charger base contains two wells, A and B, which recharge the battery pack in the Bilichék™ HHU and a spare battery pack, respectively. The two small lights on the front of the charger base (Battery Status Indicators or BSI) indicate the operation of the battery charger and battery charge status.

Clinical Summary

The goal of the study was to determine the safety and effectiveness of the Bilichek device as an indicator of serum bilirubin levels during and after phototherapy. The study design was such that infants undergoing phototherapy were entered into the study if they had at least one Bilichek measurement with a corresponding conventional serum test for bilirubin within 30 minutes of each other. In most cases, subjects also had a corresponding set of Bilichek and serum test measurements after phototherapy was discontinued. The objective of the study was to compare the results of the Bilichek instrument with blood serum bilirubin levels measured from capillary blood obtained by heel sticks, currently the most common clinical practice. The number and timing of Bilichek measurements and bloodserum tests were determined by the actual clinical indications for each subject regarding how many as well as the specific timing of when serum bilirubin measurements were made. Thus subjects often had more than one measurement pair taken during and after phototherapy.

In all cases, the predicted total serum bilirubin level from the Bilichek test (pTSB) was compared with that of actual bilirubin levels as determined by high pressure liquid chromatography (HPLC TSB) performed on serum samples collected at the time (i.e., within 30 minutes) of each Bilichek measurement.

The primary hypothesis was that the Bilichek device was accurate enough to support the claim that it could be useful for monitoring bilirubin levels during and after phototherapy. A secondary hypothesis was that there was no significant difference in accuracy between African American and Caucasian babies. The statistics used to assess accuracy were correlation coefficients, standard deviations, means of error, as well as sensitivity and specificity as compared to the gold standard of HPLC TSB. Device specifications, procedures and the linear regression model were identical to those used for the currently marketed Bilichek device previously cleared by FDA (K983071), for pre-phototherapy indications with the exception that the forehead was occluded from light using a phototherapy blocker typically used to shield the baby's eyes during phototherapy (see the User Instruction Manual amendment appended to this document).

Study Results

A total of 155 neonatal infants had at least one paired Bilichek and bilirubin serum test during phototherapy and were, therefore, enrolled in the study. Of these 165 subjects, 64 were African American, 60 were Caucasian and 31 were categorized as "other" (e.g., Hispanic, Asian, Native American). The sample size of 60 for each race was determined to assess whether a preliminary

difference in standard deviations observed was due to sampling from a limited population or an actual difference between the two races. Thus, the study population was expanded to include the 64 African American and 60 Caucasian babies in the analyses set forth below. For these 124 subjects, there were a total of 247 paired Bilichék and serum bilirubin measurements made during phototherapy and a total of 90 paired Bilichék and serum bilirubin measurements made post-phototherapy.

Safety

The Bilichék device is noninvasive and, as expected, there were no adverse events reported during the study.

Effectiveness Results

The results of the Bilichék test pTSB were compared to the gold standard HPLC TSB. High levels of correlation were found for both the during phototherapy and post-phototherapy conditions.

In order to assess whether there was a difference in Bilichék performance between the African American and Caucasian subjects during phototherapy, one measurement was selected randomly by computer to represent 30 repeated samples from the measurement.

In order to assess whether there was a difference in Bilichék performance between the African American and Caucasian subjects after phototherapy, one measurement was selected randomly by computer to represent 30 repeated samples from the measurement that had a post-phototherapy measurement pair. The standard deviation for the African American babies was 1.1520 while for the Caucasian babies it was 1.3399, a difference which was not statistically significant. However, the difference for means of error between the two races was statistically significant; pooled t-value = -2.93, $p = 0.0044$. A possible explanation for this finding may lie in the fact that in some cases i.e., post-phototherapy HPLC TSB measurements were above 12 mg/dL. However, because the absolute mean error for both races was found to be less than half a mg/dL, the clinical impact of this statistical finding is negligible.

Sensitivity and Specificity Analysis

In order to further investigate the clinical significance of the Bilichék results, the sensitivity and specificity was determined for the subjects using the same prospective criteria as in the original FDA cleared 510(k) for Bilichék. These criteria were an HPLC cut-off of 12 mg/dL and a Bilichék cut-off window of 12 (+1/-2) mg/dL. The sensitivity and specificity during phototherapy for both the African American and Caucasian subjects were very similar (sensitivity = 90.00% vs. 88.89%, respectively; and specificity =

98.15% vs. 95.24%). For post-phototherapy, specificity was 100% for both races. Even so, there were no statistically significant differences in sensitivity or specificity between the races either during or after phototherapy.

The study data indicate that the Bilichek device is effective for monitoring the progression of phototherapy both during and after successful implementation when the site being measured (the forehead) is occluded from light during phototherapy. The data supporting these conclusions are as follows:

- 1) Performance of Bilichek as measured by correlation to HPLC measurements of serum bilirubin showed that the correlation remained high both during and after phototherapy
- 2) Neither standard deviations nor means of error were statistically different when compared between African American and Caucasian subjects during phototherapy. Standard deviations post-phototherapy also were not statistically different between the two races and means of error, while statistically different, were still less than half a mg/dL for both races.
- 3) Using prospective criteria and thresholds, the Bilichek test maintained high levels of sensitivity for the during phototherapy phase and high specificity for both the during and post-phototherapy phases of the study. There were no statistically significant differences between the races regarding any of these measures.

Taken together, the results of this study support the additional claim for the safe and effective use of Bilichek for monitoring bilirubin levels during and after phototherapy by taking measurements of the forehead when it is occluded from light.

(End of Section.)



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

MAR 19 2001

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Mr. David J. Vanella
Manager, Regulatory/Product Assurance
Respironics®
1001 Murry Ridge Lane
Murrysville, Pennsylvania 15668-8550

Re: K010052
Trade Name: Respironics® Bilichek Non-Invasive Bilirubin Analyzer
Regulatory Class: I
Product Code: MQM
Dated: January 4, 2001
Received: January 8, 2001

Dear Mr. Vanella:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895.

A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

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This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsma/dsmamain.html>".

Sincerely yours,

A handwritten signature in black ink that reads "Steven Gutman". The signature is written in a cursive, slightly slanted style.

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): _____

Device Name: Respironics® Bilichek Non-Invasive Bilirubin Analyzer

Intended Use/Indications for Use

The Bilichek Non-Invasive Bilirubin Analyzer is a non-invasive transcutaneous bilirubinometer, which is intended as an index to predict serum bilirubin levels prior to phototherapy (pre-phototherapy) during and post phototherapy in neonates, without regard to gender, gestational age, or bodyweight. Neonates whose Bilichek test results are indicative of hyperbilirubinemia are evaluated by their physician(s) for appropriate patient management.

Environment of Use/Patient Population

Home or Institutional Setting / African American and Caucasian Neonates

Jean Cooper
(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K010052

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ☒
(Per 21 CFR 801.109)

OR

Over-The-Counter Use
(Optional Format 1-2-96)